This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

RECEIVED
NOV 28 2006

1. REGISTRATION NO. 41-R-0006 **CUSTOMER NO.** 542

FORM APPROVED
OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY *(Name and Address, as registered with USDA, include Zip Code)*

MAYO FOUNDATION
1997 GUGGENHEIM, 200 FIRST ST SW
ROCHESTER, MN 55905
(507) 284-1050

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS*(sites)*

See Attached Listing

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY *(Attach additional sheets if necessary or use APHIS FORM 7023A)*

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic,analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)*	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
4. Dogs	0	2	270	0	272
5. Cats	0	0	20	0	20
6. Guinea Pigs	0	39	76	188	303
7. Hamsters	0	0	0	0	0
8. Rabbits	0	110	799	0	909
9. Non-Human Primates	0	0	34	0	34
10. Sheep	3	0	37	0	37
11. Pigs	584	417	512	0	929
12. Other Farm Animals					
Goats	16	0	39	0	39
13. Other Animals					
Equine	3	0	0	0	0
Ferrets	0	6	0	0	6

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all the exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional official)

fy that the above is true, correct, and complete (7 U.S.C. Section 2143)

SIG (b)(6),(b)(7)(c) AL

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DATE SIGNED 11·27·06

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3 (Oct 88), which is obsolete

PART 1 - HEADQUARTERS

Column E Explanation

1. **Registration Number: 41-R-0006**

2. **Number of animals used in this study: 188**

3. **Species of animals used in the study. Guinea Pigs**

4. **Explain the procedure producing pain and/or distress.**

A colitis model is produced in guinea pigs by giving a single intracolonic administration of trinitrobenzene sulfonic acid (TNBS) dissolved in ethanol. This administration is done via enema with a feeding tube approximately 7 cm long in an animal anesthetized with isoflurane. A volume of 0.3-0.5 ml is administered. The ethanol will initially cause an acute inflammatory response. The TNBS creates a cell mediated immune response that can cause localized ulceration, hyperemia and edema of the colon. After administration, approximately 10% of animals do not develop lesions, 5% develop stasis with systemic effects that are euthanized, and 85% develop a localized colitis involving 20% of the entire colon. The lesions are present for up to 3 weeks. It is unclear how much pain or distress the guinea pigs experience following TNBS administration, as this has not been studied directly in this model. All animals initially lose weight due to satiety-induced decreased food intake, but almost all animals remain active and responsive and do not vocalize upon handling. If an animal shows outward signs of distress (vocalization when handled, abdominal distension, weight loss of more than 20%, or weight loss that does not recover after 4 days), the animal is immediately euthanized.

In a subgroup of guinea pigs on this colitis study, a 5 cm long midline abdominal incision is done in anesthetized guinea pigs to inject retrograde label into the prevertebral ganglia. Although buprenorphine (0.01 mg/kg s.c.) is routinely given to animals that undergo this laparotomy, it is not administered to the guinea pigs that will subsequently receive TBNS or the respective control group of this same study.

5. **Provide scientific justification why pain/and or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.**

Guinea pigs that have colitis induced by TNBS administration are not given analgesics following their recovery from the procedure. This is because available analgesics all have significant effects on gastrointestinal motility through actions on the enteric nervous system (Cowen, 2003; Kurz and Sessler, 2003), which is the system being studied in this protocol. Buprenorphine, Tramadol, and other opiates cause severe constipation, causing the administered TNBS to remain stationary in the colon that could lead to perforation, sepsis and death. The Mayo PI has first hand experience that buprenorphine (0.01 mg/kg s.c.) can exacerbate TNBS-induced intestinal inflammation and thus cause death.

Column E Explanation (Continued)
Registration Number: 41-R-0006

Anti-inflammatory agents such as acetaminophen or indomethacin can alter mucosal responses and exacerbate ulcers. Likewise, the enzyme targets of these anti-inflammatory compounds may be directly involved in the inflammatory response this laboratory seeks to study. Even newly discovered analgesics have bowel alterations that would confound the data being collected for this study, because all major neurotransmitters and most neurotransmitter receptors are located in the bowel.

In the case of guinea pigs that undergo a laparotomy incision, it would not be scientifically appropriate to compare TNBS-treated animals with no analgesics given to control animals that receive analgesics (buprenorphine). Therefore, animals that undergo the abdominal surgical procedures to retrograde label neurons in the ganglia and that are to be used as controls for TNBS-treated animals also do not receive analgesic treatment.

References:

Cowan (2003) Buprenorphine: new pharmacological aspects. Int J Clin Pract Suppl. 133:3-8.

Kurz and Sessler (2003) Opioid-induced bowel dysfunction: pathophysiology and potential new therapies. Drugs. 63:649-71.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102): None